Exhibit 3

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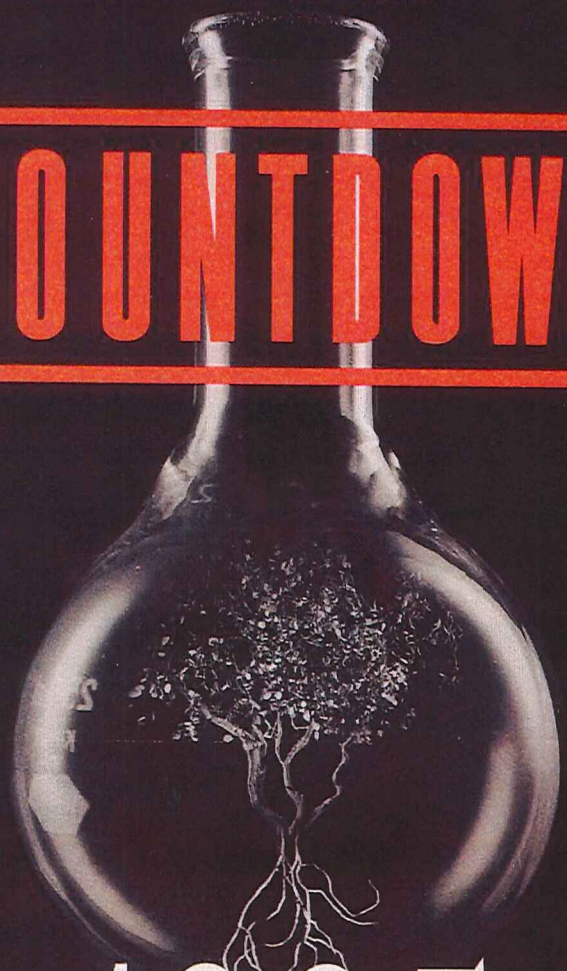
JUVENILE DIABETES FOUNDATION INTERNATIONAL • THE DIABETES RESEARCH FOUNDATION • WINTER 1995

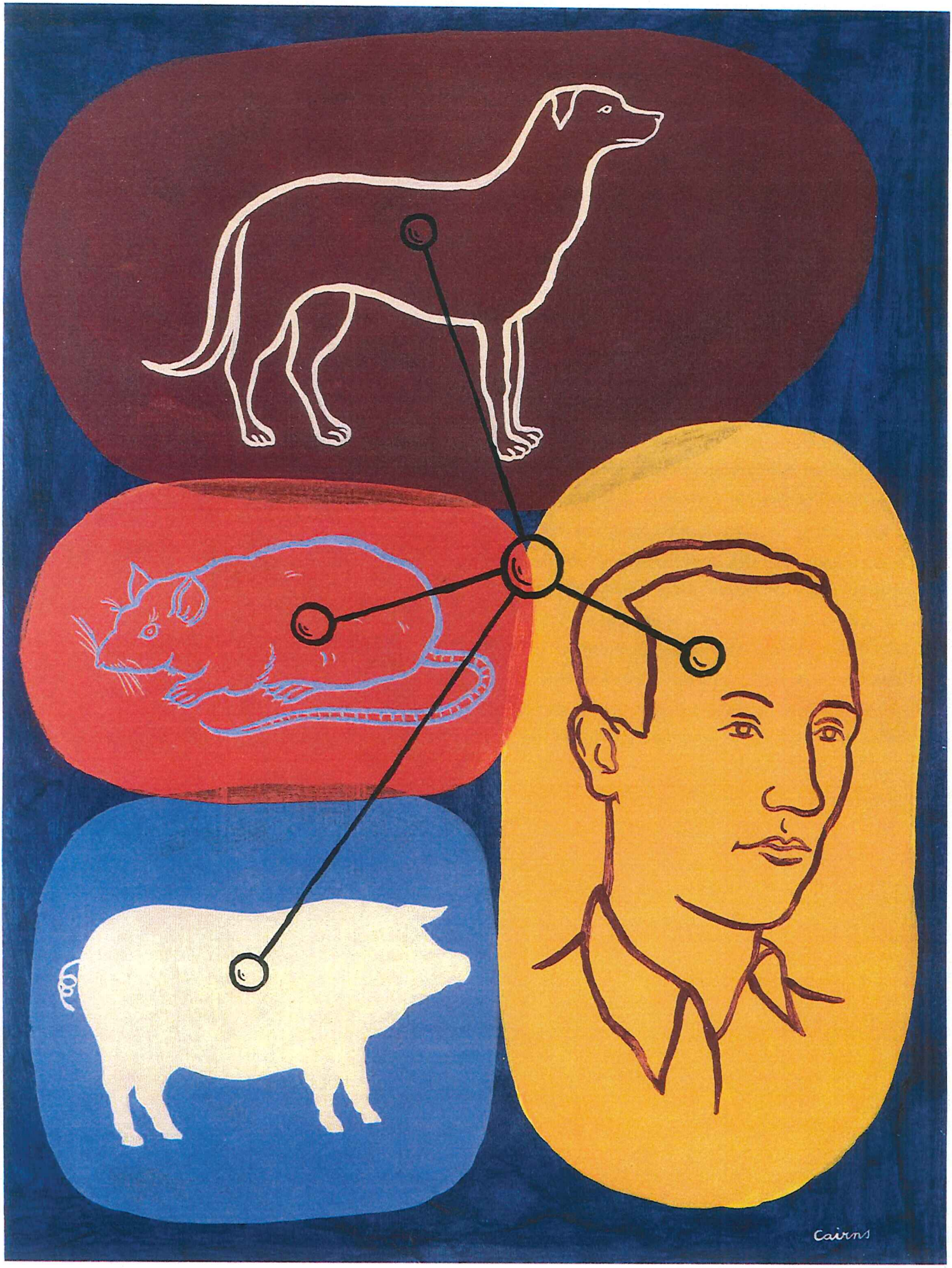
COUNTDOWN



1995 Research Progress Report

25 Years of Research Progress

1970 • A SPECIAL ANNIVERSARY ISSUE • 1995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25 YEARS of RESEARCH PROGRESS

Closing in on a Dream: THE BIOARTIFICIAL PANCREAS

Researchers look to other species to find a large supply of insulin-producing islet cells for transplantation

BY WAYNE L. CLARK

Even the most meticulous form of insulin therapy cannot mimic the precise blood sugar control afforded by a working pancreas. Doctors have been transplanting whole pancreases into people with diabetes since 1966, but because of a number of technical difficulties, whole pancreas transplantation is feasible only in a small percentage of people with diabetes receiving kidney transplants. These stumbling blocks may some day be overcome using a bioartificial pancreas, a device made of live tissue and artificial membranes, which could safely be implanted into large numbers of people with diabetes. The Juvenile Diabetes Foundation has been funding research into the bioartificial pancreas since the early 1970's. Now, more than 20 years later, such a device is fast becoming a reality as biotech firms compete to make the first commercially available bioartificial pancreas.

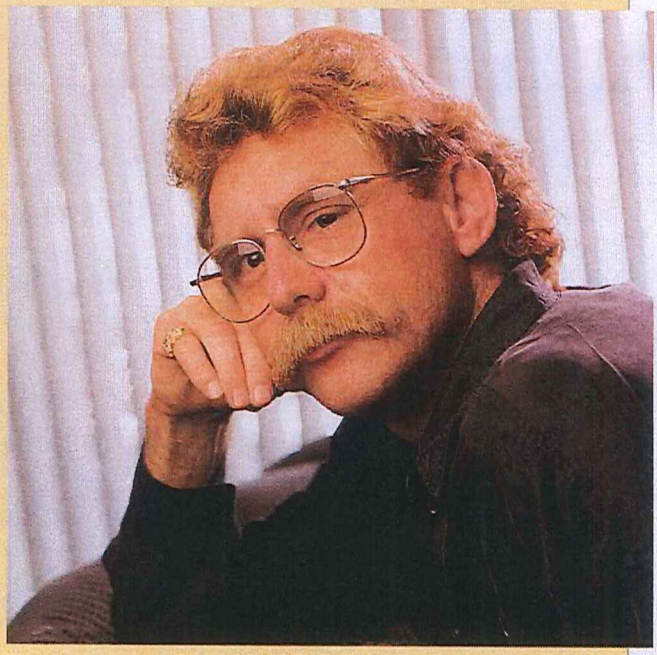
Californians Receive First Encapsulated Islet Transplants

"Just a few years ago, I was told I'd never see this in my lifetime," says 38-year-old Steven Craig. "Now I'm living it."

He is referring to the functioning islet cell transplant he received last year at Dr. Patrick Soon-Shiong's Islet Transplant Center at St. Vincent's Medical Center in Los Angeles. He has had two implantations of encapsulated islet cells, one in May and one in November, and since November he has been free of routine insulin therapy for the first time since he was eight years old. (He still requires minimal doses of insulin on some days.)

Craig has the distinction of being the first patient to ever receive a transplant of encapsulated islet cells, and the early reports are that the cells are doing as well as he is. The Anaheim, California resident, who has suffered from debilitating neuropathy in the legs, is now a walking advertisement for islet cell transplantation. "Two years ago, I was ready for a wheelchair," he says. "Now I walk five or six miles every day. The neuropathy in my legs is still there, but it's about 400 percent better."

CHRISTOPHER SPRINGMAN



Meanwhile, not too far away in the coastal city of Long Beach, Clarissa Hooper is also experiencing regression of the long-term diabetic complications that have plagued her for years. The 35-year-old received the second of Dr. Soon-Shiong's encapsulated islet cell transplants in January 1994. She is still taking some insulin, about a third of her previous dose, but already her complications are improving.

"I don't have those ups and downs anymore," she says. "My eyes are more stable, without the 'blurry days,' and I'm regaining the feeling in the bottom of my feet." Hooper has had multiple foot surgeries, and she notes that she's healing faster afterwards now.

"This gives me a chance to see my body come back after the complications from 22 years of diabetes," she says. "That alone is very comforting."

Both Steven and Clarissa are kidney transplant recipients, and so were already on medication to suppress their immune systems. Islet cell transplants have not been successful yet without the need for immunosuppressive therapy. Transplanting the encapsulated islets into these patients is the first step toward the ultimate goal, which is transplanting them without immunosuppression.

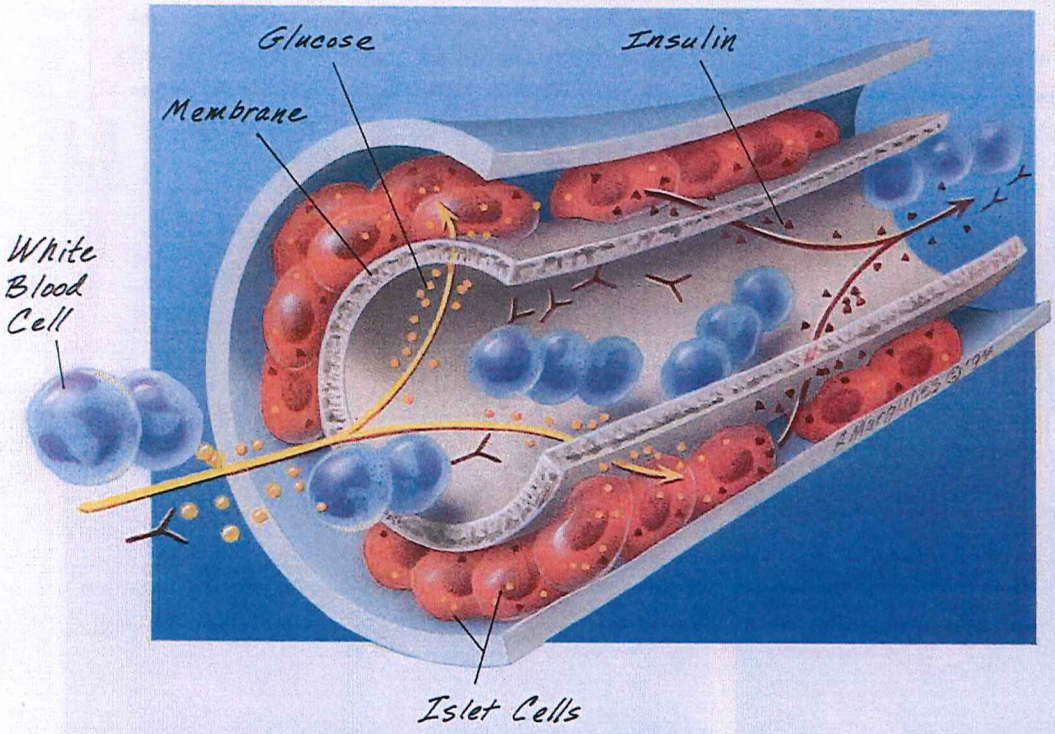
The future looks different for these two patients now. Clarissa Hooper is happy that she doesn't have to miss another season of fly fishing and that she has an easier time working. Steven Craig is going back to school so he can reenter the work force that his diabetes forced him to leave.

And Steven is spreading a message while he's at it. "I go out to speak to groups of diabetic patients," he says. "The best part is telling kids there's hope, that someone is working on it."

In transplantation, no one has yet crossed the barrier from another species to human.

many as three, pancreases to provide enough islets for one patient, the demand would outstrip the supply virtually overnight.

Scientists generally agree that the solution is an animal source of islet cells. The most likely source is the pig, which, until the advent of recombinant human insulin, was the primary source of injectable insulin for human patients. Pig insulin is strikingly similar to human insulin, differing by only one amino acid. In the United States, nearly 100 million pigs are slaughtered each year for food, and their pancreases would easily fill the need for islets for human patients.



A semipermeable membrane allows oxygen, glucose, hormones and insulin to pass through, but blocks the passage of larger molecules, especially antibodies and T cells.

ROBERT MARGULIES

The idea of transplanting tissue across species barriers, or xenotransplantation, is not without problems either. In addition to the same kind of immune response as with human islet cells, there are other immune mechanisms that protect a species from the tissue of other species. Xenotransplantation has already been performed across wide species barriers, such as rat to dog or pig to dog, but no one has yet crossed the barrier from any other species to human.

Isolating the Islets

The solution to all these problems will likely be found in the development of a device or technique that both protects the islets from the immune system and allows the necessary exchange of nutrients and insulin. This feat is made possible by a "selectively permeable" material or coating. The ideal material or coating lets oxygen, glucose, hormones, and insulin pass, but blocks passage of larger molecules – especially antibodies and the T cells of the immune system, which would destroy the islets. The material must also be inert, so that it will not trigger the body's automatic response to a foreign body. Otherwise, it would quickly be covered by a fibrous coating, effectively closing it off from the body. Currently, there are three approaches to transplantation using these materials.

One approach places islet cells inside a membrane-covered perfusion device, which is then grafted to an artery. Another method places the islet cells in a diffusion chamber made of membrane, which is then placed in a body cavity or under the skin. This technique is also called macroencapsulation. The third approach, microencapsulation, coats individual islet cells with a layer of protective material and places them in a body cavity or under the skin.

While the idea of using a barrier material to protect cells from the immune system is at least 40 years old, it was not until the 1970's that the technology was first used to reverse diabetes. In 1972, Richard Knazek, M.D., and colleagues at the National Institutes of Health reported growing cancer cells on plastic capillaries. William L. Chick, M.D., then at the Joslin Diabetes Center in Boston, adapted that technology, using beta cells instead of cancer cells, to produce a perfusion device he dubbed the "biohybrid pancreas." In 1977, he used such a device to reverse diabetes in rats. In 1980, Anthony M. Sun, M.D., of Connaught Laboratories in Toronto, also reported reversing diabetes in rats. He used islets placed inside capsules made of alginate, a material derived from seaweed. This was the first use of microencapsulation in diabetes.

St. Vincent's Medical Center

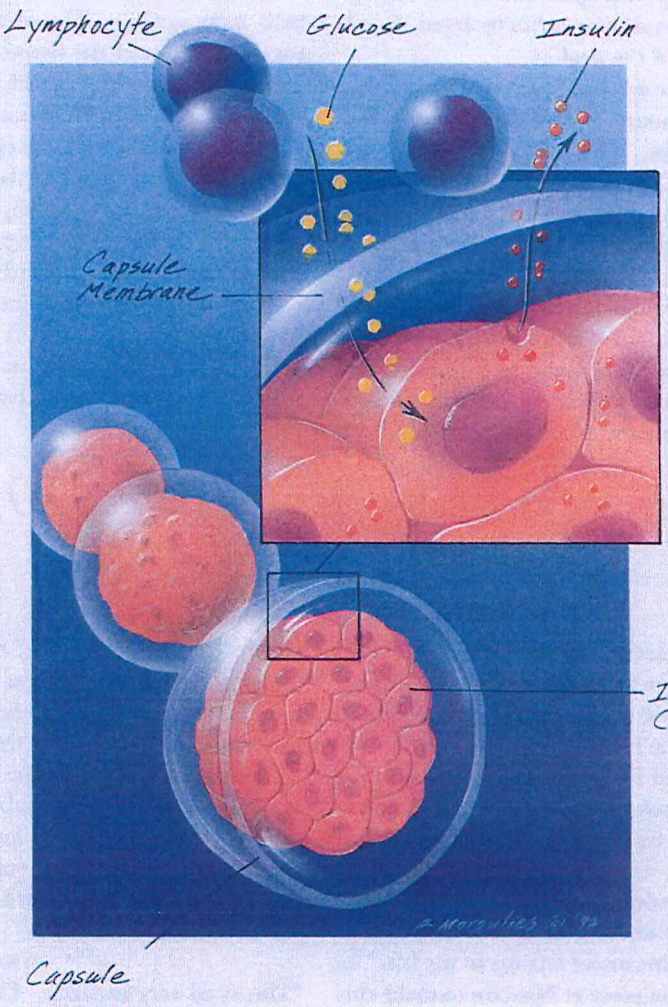
Some direct descendants of Dr. Sun's microcapsules are in Los Angeles today, in the laboratory of Patrick Soon-Shiong, M.D., at St. Vincent's Medical Center. Some of them, in fact, are in

two of Dr. Soon-Shiong's patients. He performed the first successful human transplant of encapsulated islet cells in May 1993, and a second in January 1994. One transplant recipient no longer needs injected insulin and the other requires less insulin. Both experienced some improvement in their diabetic complications following transplantation.

Dr. Soon-Shiong attributes the success of his encapsulation technique to changes in the traditional formulation of the seaweed-based alginate material. "Fibrous overgrowth of the capsule has been the major problem with this technology," he says. "We identified impurities in the formulation that were responsible for the reaction and devised a purified formula."

Dr. Soon-Shiong will now go on to transplant islets in 18 more patients with diabetes who have had transplants. Logically, the next steps would be to give transplants to patients who are not on immunosuppressive therapy, and then to use animal islets instead of human islets.

"The first clinical trial is the first step in evaluating the potential of encapsulated islets," says Dr. Soon-Shiong. "Although the transplantation of encapsulated pancreatic cells has successfully reversed diabetes in animal research studies, we have much to learn about the application of this technique to human diabetes. Only when we have fully evaluated the safety and efficacy of the technique in these FDA-approved controlled trials will we know the true potential of the therapy."



ROBERT MARGULIES

Healthy insulin-producing islet cells are encapsulated in a semipermeable membrane. Implanted under the skin, the cells are protected from immune system rejection, and work to sense glucose levels and respond with insulin production and secretion as necessary.

BioHybrid

Dr. Chick has been pursuing the bioartificial pancreas since the early 1970's. His first effort was a joint project with Amicon, the company that manufactured the plastic fibers on which he was culturing islet cells. The partnership produced a bioartificial device that was surgically connected between an artery and vein and proved somewhat successful in rat studies.

In 1986, Dr. Chick formed a biotechnology company named BioHybrid Technologies. In partnership with W.R. Grace and Company, which had acquired Amicon, he continued work on the vascular perfusion device. In its last incarnation, the device was a plastic coil about the size of a hockey puck, and it had successfully reduced the insulin requirement in dogs for up to one year.

At the same time, Chick and his colleagues were working with diffusion chambers, plastic "straws" full of islets that were implanted under the skin. Working with researchers at New England Deaconess Hospital in Boston, they had success in both small and large animals.

Now Dr. Chick has moved to a different approach, and BioHybrid and W.R. Grace have parted company. "We've looked at perfusion devices and diffusion chambers," he says. "Vascular devices require major surgery, and diffusion chambers are difficult to seal and tend to break after they're implanted."

Dr. Chick and colleagues are now looking at what they call "microreactors" – tough, resilient, spherical structures, each containing a small number of islets, that can be injected simply with a needle and syringe. According to Dr. Chick, the preclinical studies they have been performing in animals look very promising, and the animals have required no extra insulin. "The blood glucose control of these animals is really quite impressive. We're interested in approaching the FDA this year for permission to do trials in humans," he says.

Cytotherapeutics

"Competition is good," says Michael Lysaght, Ph.D. "Competition makes you hustle." Dr. Lysaght, a veteran researcher, worked with Dr. Chick on his first bioartificial pancreas as a researcher with Amicon. He is now at Cytotherapeutics, Inc., a Rhode Island biotechnology company that, until last fall, was competing in the race to develop a bioartificial pancreas.

Cytotherapeutics developed a variation of the diffusion chamber technology, called CRIB (Cellular Replacement by Immunoisolatory Biocapsule). It is using that technology to develop

treatment not only for diabetes, but for Parkinson's disease, diseases of the central nervous system such as Huntington's and Alzheimer's, and chronic pain management.

In December 1993, Cytotherapeutics made a decision that market analysts observed made "good strategic sense." It transferred its diabetes research program to California-based Neocrin, another biotechnology company seeking to be the first to market the bioartificial pancreas. Cytotherapeutics received 10 percent of Neocrin's stock as part of the deal.

"Our motivation was not that we didn't like diabetes or that we didn't have an enormous amount of confidence in developing the device," Dr. Lysaght says. "The cost of supporting trials gets to be about $10 to $20 million per product per year, and it's far better to have one or two products that are appropriately funded than several which are marginally funded or underfunded."

The first trial of the CRIB technology as applied to islet cell transplantation took place last year at Washington University in St. Louis, under the direction of Paul Lacy, M.D., and David Scharp, M.D. Dr. Scharp, who has worked with Cytotherapeutics and moved to Neocrin Company as chief scientific officer, reports that the encapsulation device protected the islets from rejection and autoimmune destruction even in Type I diabetics.

The cost of clinical trials is often $10 to $20 million a year.

Dr. Scharp, a surgeon and one of the veteran researchers in islet cell transplantation, was the first islet transplantation fellow working with Drs. Lacy and Bellinger in 1972 when they received their first grant to pursue the idea. With the objective of a practical solution in sight, he has placed his other clinical activities on hold to devote his full effort to the development of the bioartificial pancreas, dividing his time between research at Washington University and directing the scientific program at Neocrin Company. "I made this major change in my life," he says, "because the resources are in place at Neocrin to make this final objective happen."

Dr. Scharp welcomes the partnership between academia and the biotechnology industry. "I look at the enormity of what we're trying to accomplish," he says, "in terms of how much money it's going to cost to get it done. The University can't support it; the NIH can't support it. The only way to get $50 to $100 million to make it happen is with an appropriate combination of university research, commercial research, and product development."

Neocrin Company

Neocrin Company is a case study in the development of a biotechnology company. It was formed in 1992 as a joint venture between Baxter Healthcare Corporation and Trancel Corporation. Trancel, a small biotechnology firm, had developed a system for large-scale isolation and encapsulation of islets. It also had a top-flight science and research staff and a scientific advisory board.

Meanwhile, Baxter's Applied Sciences Group had developed a membrane technology that not only functioned as a selectively permeable barrier but also promoted "vascularization." It allowed new blood vessels to grow right up to the surface of the membrane, making biochemical exchanges easier and preventing the scar tissue and overgrowth that has plagued other membranes.

The two companies formed Neocrin Company as a privately held joint venture. The idea was to combine their scientific expertise and add the financial strength and ready-made distribution network of health care giant Baxter. Then, in September 1993, Neocrin became a privately held corporation, with Baxter as a major shareholder.

With the acquisition of the diabetes program from Cytotherapeutics in December 1993, Neocrin had assimilated much of the leading talent in diabetes research and all the basic technology it needed to push toward a completed bioartificial pancreas.

That device will combine encapsulated islets with a diffusion device made of Baxter's unique membrane. The company believes that this combination of microencapsulation and macroencapsulation will give the best possible mix of isolation and biochemical exchange.

According to Neocrin's CEO, Greg Dane, its researchers have completed several years of studies in small animals and are now testing scaled-up versions of the device in large animal models as a prelude to testing in humans. To accomplish that testing, Neocrin has completed a preliminary meeting with the FDA, and plans to initiate human investigational studies by the fall of this year.

A unique feature of the Neocrin device is the ability to replace islets if they lose viability over time. If this is necessary, the Neocrin system allows for a relatively simple reloading procedure wherein the device stays in place in the patient and only the islets are replaced with a fresh dose.

The Final Push

"This is all very exciting," Dane says, "because we can see how all the science is coming together to produce a practical outcome. The progress in our technical accomplishments is permitting us to actually create therapies that were only dreams just a few years back. A lot of people who have been serious researchers in this field for a long time are realizing that the final goal is within our reach."

"This is something that's been a dream of scientists for decades," says Dr. Chick. "To take a cell from an animal source, which produces substances lacking in the human patient, and give it to the patient."

The pursuit of the dream has moved from publications to patients, and soon will move from the laboratory to the marketing department. The best minds from science, development, and business have chosen up teams to vie for the first commercially available bioartificial pancreas.

It will happen soon, and the only question now seems to be exactly how soon. When it happens, as Greg Dane says, "it will be stunning."